

What is claimed is:

1. A DNA molecule comprising an isolated DNA sequence encoding a BMP-12 related protein.

2. A DNA molecule according to claim 1, wherein said DNA sequence is selected from the group consisting of:

(a) nucleotides #496, #571 or #577 to #882 of SEQ ID NO:1;

(b) nucleotides #605 or #659 to #964 of SEQ ID NO:25; and

(c) sequences which hybridize to (a) or (b) under stringent hybridization conditions and encode a BMP-12 related protein which exhibits the ability to form tendon/ligament-like tissue.

3. A DNA molecule comprising the DNA sequence of claim 1 wherein said DNA sequence is selected from the group consisting of:

(a) nucleotides encoding for amino acids #-25, #1 or #3 to #104 of SEQ ID NO:2;

(b) in a 5' to 3' direction, nucleotides encoding a propeptide selected from the group consisting of native BMP-12 propeptide and a BMP protein propeptide; and nucleotides encoding for amino acids #-25, #1 or #3 to #104 of SEQ ID NO:2; and

(c) nucleotides encoding for amino acids #1 or #19 to #120 of SEQ ID NO:26;

(d) in a 5' to 3' direction, nucleotides encoding a propeptide selected from the group consisting of native BMP-12 propeptide and a BMP protein propeptide; and nucleotides encoding for amino acids #1 or #19 to #120 of SEQ ID NO:26;

(e) sequences which hybridize to any of (a) through (d) under stringent hybridization conditions and encode a BMP-12 related protein which exhibits the ability to form cartilage and/or bone.

4. A host cell transformed with a DNA molecule according to claim 1.

5. A host cell transformed with the DNA molecule of claim 2.

6. A host cell transformed with the DNA molecule of claim 3.

7. An isolated DNA molecule having a sequence encoding a BMP-12 protein which is characterized by the ability to induce the formation of

tendon/ligament-like tissue, said DNA molecule comprising a DNA sequence selected from the group consisting of:

- (a) nucleotide #496, #571 or #577 to #882 of SEQ ID NO:1;
- (b) nucleotide #605 or #659 to #964 of SEQ ID NO:25; and
- (c) naturally occurring allelic sequences and equivalent degenerative codon sequences of (a) or (b).

8. A host cell transformed with the DNA molecule of claim 7.

9. A vector comprising a DNA molecule of claim 7 in operative association with an expression control sequence therefor.

10. A host cell transformed with the vector of claim 9.

11. A method for producing a purified BMP-12 protein, said method comprising the steps of:

(a) culturing a host cell transformed with a DNA molecule according to claim 2, comprising a nucleotide sequence encoding a BMP-12 related protein; and

(b) recovering and purifying said BMP-12 related protein from the culture medium.

12. A method for producing a purified BMP-12 related protein said method comprising the steps of:

(a) culturing a host cell transformed with a DNA molecule according to claim 3, comprising a nucleotide sequence encoding a BMP-12 related protein; and

(b) recovering and purifying said BMP-12 related protein from the culture medium.

13. A method for producing a purified BMP-12 related protein said method comprising the steps of:

(a) culturing a host cell transformed with a DNA molecule according to claim 7, comprising a nucleotide sequence encoding a BMP-12 related protein; and

(b) recovering and purifying said BMP-12 related protein from the culture medium.

14. A purified polypeptide comprising an amino acid sequence selected from the following group:

(a) from amino acid #-25 to amino acid #104 as set forth in SEQ ID NO:2;

5 (b) from amino acid #1 to amino acid #104 as set forth in SEQ ID NO:2.

(c) from amino acid #3 to amino acid #104 as set forth in SEQ ID NO:2.

(d) from amino acid #1 to amino acid #120 as set forth in SEQ ID NO:26; and

10 (d) from amino acid #19 to amino acid #120 as set forth in SEQ ID NO:26.

15 15. A purified polypeptide wherein said polypeptide is in the form of a dimer comprised of two subunits, each with the amino acid sequence of claim 14.

16. A purified protein produced by the steps of

15 (a) culturing a cell transformed with a DNA molecule comprising the nucleotide sequence from nucleotide #496, #571 or #577 to #882 as shown in SEQ ID NO:1; and

20 (b) recovering and purifying from said culture medium a protein comprising the amino acid sequence from amino acid #-25, amino acid #1 or amino acid #3 to amino acid #104 as shown in SEQ ID NO:2.

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17. A purified BMP-12 related protein characterized by the ability to induce the formation of tendon/ligament-like tissue.

25 18. A pharmaceutical composition comprising an effective amount of the BMP-12 related protein of claim 17 in admixture with a pharmaceutically acceptable vehicle.

19. A method for inducing tendon/ligament-like tissue formation in a patient in need of same comprising administering to said patient an effective amount of the composition of claim 18.

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30 20. A pharmaceutical composition for tendon/ligament-like tissue healing and tissue repair said composition comprising an effective amount of the protein of a BMP-12 related protein in a pharmaceutically acceptable vehicle.

21. A method for treating tendinitis, or other tendon or ligament defect in a patient in need of same, said method comprising administering to said patient an effective amount of the composition of claim 20.

22. A chimeric DNA molecule comprising a DNA sequence encoding a propeptide from a member of the TGF- β superfamily of proteins linked in correct reading frame to a DNA sequence encoding a BMP-12 related polypeptide.

23. A chimeric DNA molecule according to claim 22, wherein the propeptide is the propeptide from BMP-2.

24. A heterodimeric protein molecule comprising one monomer having the amino acid sequence of the polypeptide of claim 14, and one monomer having the amino acid sequence of a protein of the TGF- β superfamily.

25. A method for inducing tendon/ligament-like tissue formation in a patient in need of same comprising administering to said patient an effective amount of a composition comprising a protein encoded by a DNA sequence selected from the group consisting of:

- (a) nucleotides #496, #571 or #577 to #882 of SEQ ID NO:1;
- (b) nucleotides #845 or #899 to #1204 of SEQ ID NO:3;
- (c) nucleotides #605 or #659 to #964 of SEQ ID NO:25; and
- (d) sequences which hybridize to (a), (b) or (c) under stringent hybridization conditions and encode a protein which exhibits the ability to form tendon/ligament-like tissue.

26. A method for inducing tendon/ligament-like tissue formation in a patient in need of same comprising administering to said patient an effective amount of the composition comprising a tendon/ligament-like tissue inducing protein having an amino acid sequence selected from the group consisting of:

- (a) amino acids #-25, #1 or #3 to #104 of SEQ ID NO:2;
- (b) amino acids #1 or #19 to #120 of SEQ ID NO:4;
- (c) amino acids #1 or #19 to #120 of SEQ ID NO:26; and
- (d) mutants and/or variants of (a), (b) or (c) which exhibit the ability to form tendon and/or ligament.

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27. A pharmaceutical composition for tendon/ligament-like tissue repair, said composition comprising an effective amount of a BMP-12 related protein in a pharmaceutically acceptable vehicle.

5 28. A method for treating tendinitis, or other tendon or ligament defect in a patient in need of same, said method comprising administering to said patient an effective amount of the composition of claim 27.

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